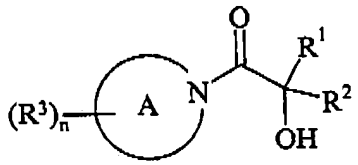
IN THE CLAIMS:

a'

1 (**currently amended and reformatted**): A compound of formula (I):



(I)

wherein:

Ring A is ~~a nitrogen linked mono or bicyclic heterocyclic ring; wherein if said heterocyclic group contains an -NH- moiety that nitrogen is~~ piperazinyl optionally substituted on nitrogen by R^4-D-;

R^1 and R^2 are independently $C_k$alkyl optionally substituted by 1 to 2k+1 atoms selected from fluoro and chloro wherein k is 1-3;

or R^1 and R^2 together with the carbon atom to which they are attached, form a $C_m$cycloalkyl ring optionally substituted by 1 to 2m-2 fluorine atoms wherein m is 3-5;

R^3 is a substituent on carbon and is halo, hydroxy, cyano, formyl, amino, nitro, carboxy, carbamoyl, ureido, thiol, sulphamoyl or R^5-E-;

R^4 is C_{1-6}alkyl, phenyl or a heterocyclic group, wherein in R^4 any C_{1-6}alkyl, phenyl or heterocyclic groups (on a ring carbon) may be optionally substituted by one or more R^6 and if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^8;

D is -C(O)-, -N(R^9)C(O)-, -S(O)$_2$-, -NS(O)$_2$-, -OC(O)- or D is a direct bond;

R^5 is C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, phenyl, naphthyl or a heterocyclic group, wherein in R^5 any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl, phenyl, naphthyl or heterocyclic groups (on a ring carbon) may be optionally substituted by one or more R^6 and if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^8;

E is -O-, -N(R^9)-, -C(O)-, -N(R^9)C(O)-, -C(O)N(R^9)-, -S(O)$_a$- wherein a is 0-2, -OC(O)-, -C(O)O-, -N(R^9)C(O)O-, -OC(O)N(R^9)-, -C(S)N(R^9)-, -N(R^9)C(S)-, -SO$_2$N(R^9)-,

$-N(R^9)SO_2-$, $-N(R^9)C(O)N(R^9)-$, $-N(R^9)C(S)N(R^9)-$, $-SO_2NHC(O)-$, $-SO_2N(R^9)C(O)-$, $-C(O)NHSO_2-$ or E is a direct bond;

a'

R^6 is trifluoromethyl, C_{1-6}alkyl, halo, hydroxy, trifluoromethoxy, cyano, C_{1-6}alkoxy, formyl, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, *N*-(C_{1-6}alkyl)amino, *N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, C_{1-6}alkanoyl(*N*-C_{1-6}alkyl)amino, nitro, carboxy, carbamoyl, C_{1-6}alkoxycarbonyl, thiol, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, C_{1-6}alkylsulphonylamino, sulphamoyl, *N*-(C_{1-6}alkyl)aminosulphonyl, *N*-(C_{1-6}alkyl)$_2$aminosulphonyl, *N*-(C_{1-6}alkyl)carbamoyl, *N*-(C_{1-6}alkyl)$_2$carbamoyl, ureido, *N'*-(C_{1-6}alkyl)ureido or *N'*-(C_{1-6}alkyl)$_2$ureido, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{3-6}cycloalkyl, naphthyl, phenyl or a heterocyclic group wherein in R^6 any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cylcoalkyl, naphthyl, phenyl or heterocyclic groups (on a ring carbon) may be optionally substituted by one or more R^7 and if said heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^8;

R^7 is trifluoromethyl, cyano, C_{1-6}alkyl, halo, hydroxy, trifluoromethoxy, C_{1-6}alkoxy, formyl, C_{1-6}alkanoyl, C_{1-6}alkanoyloxy, amino, *N*-(C_{1-6}alkyl)amino, *N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, C_{1-6}alkanoyl(*N*-C_{1-6}alkyl)amino, nitro, carboxy, carbamoyl, C_{1-6}alkoxycarbonyl, thiol, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, C_{1-6}alkylsulphonylamino, sulphamoyl, *N*-(C_{1-6}alkyl)aminosulphonyl, *N*-(C_{1-6}alkyl)$_2$aminosulphonyl, *N*-(C_{1-6}alkyl)carbamoyl, *N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{2-6}alkenyl, C_{2-6}alkynyl, C_{3-6}cycloalkyl or a heterocyclic group (optionally substituted by one or more R^{11}), and wherein in R^7 any C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl or C_{3-6}cylcoalkyl groups may be optionally substituted by one or more groups selected from R^{12};

R^8 is C_{1-6}alkyl, C_{1-6}alkanoyl, C_{1-6}alkylsulphonyl, C_{1-6}alkoxycarbonyl, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, benzoyl, (heterocyclic group)carbonyl, phenylsulphonyl, (heterocyclic group)sulphonyl, phenyl or a carbon linked heterocyclic group, and wherein in R^8 any C_{1-6}alkyl, phenyl or heterocyclic group (on a ring carbon) may be optionally substituted by one or more R^6, and if a heterocyclic group contains an -NH- moiety that nitrogen may be optionally substituted by a group selected from R^{11};

R^9 is hydrogen or C_{1-6}alkyl optionally substituted by one or more R^{10} with the proviso that R^{10} is not a substituent on the carbon attached to a nitrogen atom;

R^{10} is halo, hydroxy, amino, cyano, nitro, trifluoromethyl, trifluoromethoxy, C_{1-6}alkyl, C_{2-6}alkenyl, C_{2-6}alkynyl, *N*-(C_{1-6}alkyl)amino, *N*-(C_{1-6}alkyl)$_2$amino, C_{1-6}alkanoylamino, C_{1-6}alkanoyl(*N*-C_{1-6}alkyl)amino, C_{1-6}alkylsulphonylamino, C_{1-6}alkylsulphonyl(*N*-C_{1-6}alkyl)amino, thiol, C_{1-6}alkylsulphanyl, C_{1-6}alkylsulphinyl, C_{1-6}alkylsulphonyl, sulphamoyl, *N*-(C_{1-6}alkyl)aminosulphonyl, *N*-(C_{1-6}alkyl)$_2$aminosulphonyl, carboxy, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxycarbonyl, C_{1-6}alkanoyl or formyl;

R^{11} is C_{1-6}alkyl, C_{1-6}alkanoyl, C_{1-6}alkylsulphonyl, C_{1-6}alkoxycarbonyl, carbamoyl, *N*-(C_{1-6}alkyl)carbamoyl, *N,N*-(C_{1-6}alkyl)$_2$carbamoyl, C_{1-6}alkoxyC_{1-6}alkanoyl, phenylC_{1-6}alkyl, benzoyl, phenylC_{1-6}alkanoyl, phenylC_{1-6}alkoxycarbonyl or phenylsulphonyl and wherein in R^{11} any C_{1-6}alkyl group can be optionally substituted by one or more R^{13};

R^{12} is halo, hydroxy, *N*-methylpiperazinyl, *N*-acetylpiperazinyl, morpholino, piperidino, cyano, amino, *N,N*-dimethylamino, acetamido, carbamoyl, carboxy, methanesulphonyl or sulphamoyl;

R^{13} is halo, hydroxy, cyano, amino, *N,N*-dimethylamino, acetamido, carbamoyl, carboxy, methanesulphonyl or sulphamoyl;

n is 0-5; wherein the values of R^3 may be the same or different;

or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof;

with the proviso that if R^1 is methyl, R^2 is trifluoromethyl and Ring A is piperazin-1-yl then $(R^3)_n$ is not i) 4-cyanobenzoyl, ii) 2-methyl-4-benzyloxycarbonyl, iii) 2-methyl, iv) 2-methyl-4-cyanobenzoyl, v) 2,5-dimethyl-4-benzyl, vi) 2,5-dimethyl or vii) 2,5-dimethyl-4-cyanobenzoyl.

2 (**original**): A compound of formula (**I**) according to claim 1 wherein one of R^1 and R^2 is methyl and the other is trifluoromethyl;

or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

a1

3 (**cancelled**).

4 (**currently amended**): A compound of formula (**I**) according to claim 1 ~~any one of claims 1 to 3~~ wherein R^3 is a substituent on carbon and is selected from amino, methyl, 4-mesylphenylsulphonyl, 4-methylthiophenylthio, 4-fluorobenzoyl and 4-cyanobenzoylamino;
or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

5 (**currently amended**): A compound of formula (**I**) according to claim 1 ~~any one of claims 1 to 4~~ wherein R^4 is C_{1-4}alkyl, phenyl {optionally substituted with one or more *t*-butyl, isopropyl, nitro, halo, *N,N*-dimethylcarbamoyl, *N,N*-dimethylamino, 2-hydroxyethylamino, cyano, acetyl, methoxy or carboxy} or thienyl;
or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

6 (**currently amended**): A compound of formula (**I**) according to claim 1 ~~any one of claims 1 to 5~~ wherein D is $-SO_2-$ or -C(O)-;
or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

7 (**currently amended**): A compound of formula (**I**) according to claim 1 ~~any one of claims 1 to 6~~ wherein n is 0 - 3;
or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

8 (**original; reformatted**): A compound of formula (**I**) selected from:
(R)-[(2S,5R)-2-methyl-5-methyl-4-(4-carboxyphenylsulphonyl)-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropionyl)piperazine];
(R)-[(2S,5R)-2-methyl-5-methyl-4-(4-dimethylcarbamoylphenylsulphonyl)-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropionyl)piperazine];
(R)-[(2S,5R)-2-methyl-5-methyl-4-(4-fluorophenylsulphonyl)-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropionyl)piperazine];

(R)-{(2S,5R)-2-methyl-5-methyl-4-[4-(2-hydroxyethylamino)phenylsulphonyl]-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropionyl)piperazine};

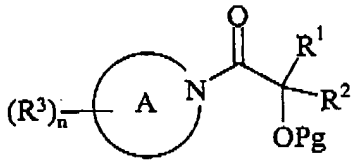
(R)-[(2S,5R)-2-methyl-5-methyl-4-(4-cyanophenylsulphonyl)-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropionyl)piperazine]; and

(R)-[(2S,5R)-2-methyl-5-methyl-4-(4-methoxyphenylsulphonyl)-1-(3,3,3-trifluoro-2-hydroxy-2-methylpropionyl)piperazine];

or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof.

9 (**currently amended and reformatted**): A process for preparing a compound of formula (**I**) or a pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof, which process (in which variable groups are as defined in claim 1 for formula (**I**) unless otherwise stated) comprises of:

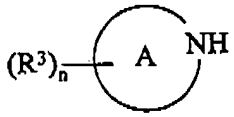
(a) deprotecting a protected compound of formula (**II**):



(**II**)

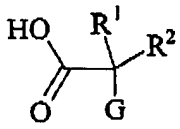
where Pg is an alcohol protecting group;

(b) coupling an amine of formula (**III**):



(**III**)

with an acid of formula (**IV**):



(**IV**)

wherein G is a hydroxyl group;

(c) coupling an amine of formula (**III**) with an activated acid derivative of formula (**IV**)

wherein G is a hydroxyl group which may be protected as an ester or ether;

and thereafter if necessary:

i) converting a compound of the formula **(I)** into another compound of the formula **(I)**;

ii) removing any protecting groups; or

iii) forming a pharmaceutically acceptable salt or *in vivo* hydrolysable ester.

10 (**currently amended**): A pharmaceutical composition which comprises a compound of formula **(I)** according to any one of claims 1-2 and 4-8~~1—8~~, or a pharmaceutically acceptable salt or *in vivo* hydrolysable ester thereof in association with a pharmaceutically-acceptable diluent or carrier.

Claims 11-12 (**cancelled**).

Claim 13 (**new**): A method for the treatment of a disease state associated with reduced PDH activity, said method comprising administering to a warm-blooded animal in need thereof a PDH activity-elevating amount of a compound of the formula (I) or pharmaceutically acceptable salt or an *in vivo* hydrolysable ester thereof, as claimed in any one of claims 1–2 and 4-8.

Claim 14 (**new**): The method of claim 13 wherein said disease state is selected from the group consisting of diabetes mellitus, peripheral vascular disease and myocardial ischaemia.

Claim 15 (**new**): The method of claim 14 wherein said disease state is diabetes mellitus.